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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/355,214	07/23/1999	ANDREW C. CHAN	A-64383-2	6140

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EXAMINER	
ZITOMER, STEPHANIE W	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 02/13/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/355,214	Applicant(s) CHAN et al.
	Examiner S. Zitomer	Art Unit 1655

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Nov 8, 2001* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *35-45* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *35-45* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

Application status

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on November 8, 2001 has been entered. Receipt of the Response and Amendment, oath/declaration and 132 declaration of inventor Chan filed with the RCE request is acknowledged.

2. Applicant's cancelation of all previously pending claims, 23-34, and presentation of new claims 35-45 in paper no. 11 filed November 8, 2001 is acknowledged.

3. Rejections not reiterated herein from the previous final Office action, paper no. 7 mailed December 8, 2000, if any, have been withdrawn in view of cancelation of the previously pending claims. Otherwise, such rejections have been applied to the new claims. All of applicant's arguments have been considered.

Objection to the specification

4. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: applicant has not pointed out support for the new subject matter in claims 37, 38 and 41.

Defective oath

5. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02. The oath or declaration is defective because it is not signed by inventor Fu. Applicant's intention to file a new declaration containing Fu's signature is acknowledged.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Rejections under 35 U.S.C. 101 and 112, first paragraph: Lack of utility and enablement

6. Claims 35-45 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility. The nature of the claimed invention is such that the activity of the BLNK protein has not been defined and is largely speculative based on the ability to bind other B cell proteins. The specification teaches that the claimed BLNK protein interacts with various B cell proteins including Grb2, PLCγ, nck, Vav and phospholipase C following BCR activation (page 19). It is stated further that a function of BLNK "is to modulate the ability of the B cell receptor to regulate calcium levels in the cell" (page 19, lines 7-9). However, modulation of BCR regulation of calcium levels is not shown to be a factor in any disease or condition identifiable or treatable with a BLNK protein nor has any other disease or condition been shown to be associated with the activity of a BLNK protein. Therefore, the asserted utility is a general utility, not a specific utility for treating or diagnosing a specific disease or condition. Furthermore, the asserted utility of BLNK proteins as specific B-cell markers (page 19, lines 19-23) is also a general utility because the finding that they are more highly expressed in B-cells relative to other cell types is not novel in that other proteins can be used as B-cell specific markers in the same way. Note that because the claimed invention is not supported by a specific asserted utility credibility cannot be assessed.

7. Claims 35-45 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Response to applicant's arguments traversing lack of utility and enablement rejections

8. Applicant's arguments filed November 8, 2001 have been fully considered but they are not persuasive. Arguments regarding the credibility of the claimed invention are irrelevant to the rejections which do not raise this issue. The "note" at the end of the 101 rejection, which states, "because the claimed invention is not supported by a specific asserted utility credibility cannot be assessed", clearly establishes that **it has not been possible** to consider the plausibility of the claimed invention absent an assertion of specific

and substantial utility. The "characteristics and functions" of BLNK cited in the arguments are just that and do not constitute a utility.

Response to declaration under 37 CFR 1.132 of inventor Chan

9. The declaration of inventor Chan filed November 1, 2001 has been fully considered but it is not persuasive. Inventor Chan expresses disagreement "with the Examiner's position that the specification does not support a specific and substantial utility for the claimed BLNK protein compositions". However, the declaration fails to cite any specific and substantial utility in the specification but, as in the arguments above, points out "characteristics and functions for BLNK proteins" which are alleged to "indicate that the claimed BLNK protein compositions have utility". No explanation or supporting evidence is provided. The declaration goes on to state disagreement with a "position" incorrectly attributed to the examiner, which inventor Chan expresses as "publications of record (attached hereto) concerning BLNK protein functions". However, the attached publications of Pappu et al. and Minigeshi et al. were published in December of 1999, almost three years after the filing of the application and thus are not available as proper references. *In re Koller*,613 F.2d 819, 823 n. 5, 204 USPQ 702, 706 n. 5 (CCPA 1980). Furthermore, the declaration, while claiming that the publications support assertions in the specification that BLNK proteins have specific and substantial utility, fails to point out any nexus in the specification between such assertions therein and the cited hypogammaglobulinemia discussed in Minigeshi et al..

Rejection under 35 U.S.C. 112, first paragraph: New matter

10. Claim 38 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claim is drawn to a BLNK protein of claim 35 or 37 comprising "an amino acid sequence which lacks at least one tyrosine phosphorylation site corresponding to a tyrosine phosphorylation site selected from [group of five sites] in SEQ ID NO:1". The specification does not describe this protein. The tyrosine phosphorylation sites are set out at page 6 and at page 16 substitution and deletion variants are discussed in general, stating that preferred deletion variants include one or more of the

three BLNK protein domains. At page 18 the specification notes that one or more of the tyrosine phosphorylation sites may be altered and provides the example of a mutant BLNK protein in which all five sites are replaced with phenylalanine. Deletion of individual phosphorylation sites is not described.

Rejection under 35 U.S.C. 112, first paragraph: Lack of written description

11. Claims 35-45 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are drawn to a very large genus of recombinant BLNK protein species comprising the protein of SEQ ID NO:1, species of protein comprising an amino acid sequence at least 95% identical to SEQ ID NO:!, species of nucleic acids encoding the protein and species of antibodies to the protein. In addition to enablement the first paragraph of 112 requires a "written description". As set forth by the Court in *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111, the written description must convey to one of skill in the art "with reasonable clarity" that as of the filing date applicant was in possession of the claimed invention. The specification describes the protein, BLNK1, and its splice variant, BLNK2, and discloses the amino acid sequence of BLNK1 (SEQ ID NO:1) as well as the nucleotide sequence encoding it (SEQ ID NO:2). However, the specification is silent regarding the sequences of other BLNK protein and nucleic acid species to which the claims are drawn. The specification does not describe any of the large number of nucleic acids and peptide species encompassed by the claims which encode a recombinant BLNK protein comprising SEQ ID NO:1 or which have at least 95 percent identity to these nucleotide and amino acid sequences as well as the claimed methods, compositions and antibodies involving the nucleic acid and amino acid sequence species encompassed by the claims. The claims encompass a very large number of nucleic acids and proteins only one of which in each category is disclosed. The specification states at page 5 that nucleic acids and proteins having a given percent homology may be "determined using standard techniques known in the art, such as the Best Fit program... or the BLASTX program" and that "alignment may include the introduction of gaps in the sequences to be aligned". This loose description of how the claimed sequences may be found does not provide sufficient

teaching or guidance to enable one skilled in the art to determine the specific sequences that are within the scope of the claims. No specific algorithm used for alignment nor the Gap or Gap Extension Penalties is disclosed. At page 15 the specification states that the invention includes "amino acid sequence variants" of three types: "substitutional, insertional or deletional" and may be "fragments" of BLNK proteins (lines 20-29). Pages 16-17 discuss the kinds of amino acid substitutions that may be brought about by mutation but no teaching or guidance is provided as to which residues of the proteins may be substituted or deleted or which amino acids are to be inserted at which positions. For example, in a 456 amino acid sequence comprising 95% identity to SEQ ID NO:1, 23 residues may be removed *en bloc* from either terminus or from any internal position or 23 residues may be changed at indeterminate positions along the length of the protein. Similarly, in a 1086 nucleotide sequence, 90 nucleotides may be changed whereas no guidance is provided for determining the nucleotide positions to be altered. The court stated in *Amgen, Inc.* v. *Chugai Pharmaceutical Co. Ltd*, 18 USPQ2d, 1016,

> Conception of chemical compound requires that inventor be able to define compound so as to distinguish it from other materials, and to describe how to obtain it, rather than simply defining it solely by its principal biological property; thus, when inventor of gene, which is a chemical compound albeit a complex one, is unable to envision detailed constitution of gene so as to distinguish it from other materials, as well as method for obtaining it, conception is not achieved until reduction to practice has occurred, and until after gene has been isolated.

Further, the specification states at page 15 that "rabbit polyclonal" and "mouse monoclonal" antibodies to BLNK fusion proteins were made. However, these antibodies are not described: not as to their type nor the epitopes to which they bind nor the procedures by which they were made. Absent description of a representative number of nucleic acid, polypeptide and antibody species the specification cannot convey to one of skill in the art that applicant possessed the large genus of claimed nucleotide and amino acid sequences and antibodies as of the date the application was filed. **This rejection may be overcome by**

limiting the claims to recombinant BLNK proteins having the specific functions characteristic of the proteins as described in the specification, pages 6 and 20, as cited at page 5 of the Response.

Rejection under 35 U.S.C. 112, second paragraph: Indefiniteness

12. Claims 1-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) Claims 37, 41, 43-45 and claims dependent therefrom lack positive real time definition because the phrase "will bind" refers to a future event.

(b) In claim 45, it is unclear whether "is capable of" describes a method step or a property of the protein.

~~Dould~~ Double patenting obviousness-type rejection

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. Claims 35-37 and 39-42 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 5,994,522. Although the conflicting claims are not identical, they are not patentably distinct from each other because the patent claims are drawn to a recombinant nucleic acid and host cell transformed therewith wherein the nucleic acid encodes the protein of the application claims and wherein the nucleic acids and the proteins have the same sequences in both sets of claims. It would have been obvious to the skilled practitioner in the art to

provide the protein of the application claims via expression of the recombinant nucleic acid in the host cell of the patent claims as routinely practiced in the art for the benefit making a sufficient amount of protein for study. It would have been obvious further to provide nucleic acids and proteins having 95% identity to the orignally isolated nucleic acid and protein as routinely practiced in the art for the benefit of implementing structure-function studies.

Conclusion

14. No claim is allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephanie Zitomer whose telephone number is (703) 308-3985. The examiner can normally be reached on Monday through Friday from 9:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152. The official fax phone number for this Group is (703) 308-4242. The unofficial fax number is (703) 308-8724.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Stephanie Zitomer, Ph.D.
February 7, 2002